

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference B0801/7169WO		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/08586	International filing date (day/month/year) 31/03/2000	Priority date (day/month/year) 02/04/1999	
International Patent Classification (IPC) or national classification and IPC A61K31/7088			
Applicant THE BRIGHAM AND WOMEN'S HOSPITAL, INC.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 11 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 28/09/2000	Date of completion of this report 29.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Peris Antoli, B Telephone No. +49 89 2399 8476 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/08586

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-51 as originally filed

Claims, No.:

1-59 as originally filed

60-144 as received on 25/01/2001 with letter of 25/01/2001

Drawings, sheets:

1/10-7/10,9/10, 10/10 as originally filed

8/10 as received on 21/06/2000 with letter of 19/06/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

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4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

- ☐ copy of the earlier application whose priority has been claimed.
- ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-108,112,113,116,120,123,125-135,137,142,143 (completely);
109-111,114,115,117-119,121,122,124,136,138-141,144 (partially);
109-111,114,115,117-119,121,122,124,136,138-141,144 (industrial applicability) .

because:

- ☒ the said international application, or the said claims Nos.
109-111,114,115,117-119,121,122,124,136,138-141,144 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

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- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos.
1-108,112,113,116,120,123,125-135,137,142,143 (completely);
109-111,114,115,117-119,121,122,124,136,138-141,144 (partially).

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	109-111,114,115,117-119,121,122,124,136,138-141,144
	No:	Claims	
Inventive step (IS)	Yes:	Claims	109-111,114,115,117-119,121,122,124,136,138-141,144
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	109-111,114,115,117-119,121,122,124,136,138-141,144 (see separate sheet)
	No:	Claims	

**2. Citations and explanations
see separate sheet**

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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EXAMINATION REPORT - SEPARATE SHEET**

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Re Item II

Priority

1. This opinion is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document Tzianabos, A. et al.: ABSTRACTS OF THE 99 TH GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, CHICAGO, US, MAY 30-JUNE 3, 1999, vol. 99, - 3 June 1999 (1999-06-03) pages 37-38, WASHINGTON, US, cited in the international search report could become relevant, to assess whether the claimed subject matter satisfies the criteria set forth in Article 33(1) PCT. ✓ AWS

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. The present claims 1-144 correspond to original claims 1-64 and 67-146. As indicated in the international search report (see Form PCT/ISA/210 Box. I.2), the search of the original claims 1-64 and 67-146 has been limited to those parts relating to the compounds specified in examples 2-9 and 12-14; i.e. *Bacteroides fragilis* capsular polysaccharide A (PS A), *Streptococcus pneumonia* type 1 capsular polysaccharide (CP) and (K-D)_n peptides.
 - 2.1 *B. fragilis* PS A and *S. pneumonia* type 1 CP have a molecular weight greater than 50 kilodaltons (see description: p. 15, I. 24-25, wherein it is indicated that *B. fragilis* PS A is composed of approx. 200 tetrasaccharide units - which will result in a molecular weight of approx. 165 kDa; and p. 50, I. 8-10 wherein it is indicated that *S. pneumonia* type 1 CP has a molecular weight of 80 kDa). Because of their molecular weight and polysaccharide nature said *B. fragilis* PS A and *S. pneumonia* type 1 CP do not fall within the scope of polymers defined in the present independent claims 1, 19, 37, 61, 63, 65, 99, 101, 102, 104 and 106 and 125. The same applies to the dependent claims 2-18, 20-36, 38-60, 62, 64, 66-98, 100, 103, 105, 107-108 and 126-135. Furthermore, the referred polysaccharides do not fall within the scope of the polymers covered by the present dependent claims 112-113, 116, 120, 123, 137, 142 and 143.

- 2.2 The (K-D)₁₋₂₅ peptides disclosed in examples 4-5 of the present application consist of repeating K-D units having a charge motif composed of positively charged free amino moiety (in the lysin (K)) and a negative charge (in aspartic acid (D)). The positive charge of the repeating units (or charge motifs) are separated from each other only by one negatively charged amino acid, namely the aspartic acid. It is hence apparent that the distance between the positively charged free amino moieties of two repeating K-D units will be less than 32Å . The referred K-D peptides do therefore not fall within the scope of polymers defined the present independent claims 1, 19, 37, 61, 63, 65, 99, 101, 102, 104, 106, 109, 125 and 136. The same applies to the dependent claims 2-18, 20-36, 38-60, 62, 64, 66-98, 100, 103, 105, 107-108, 110-124, 126-135 and 137-144.
- 2.3 According to Rule 66.1(e) PCT, no international preliminary examination will be carried out in respect of the subject matter which is not covered by the search report.
Hence no opinion will be given regard to novelty, inventive step and industrial applicability of the present claims 1-108, 112-113, 116, 120, 123, 125-135, 137, 142 and 143.
- 2.4 Concerning claims 109-111, 114-115, 117-119, 121-122, 124, 136, 138-141 and 144, only a partial opinion will be given; namely, as far as said claims encompass the polysaccharides *B. fragilis* PS A and *S. pneumonia* type 1 CP.
3. Claims 109-111, 114-115, 117-119, 121-122, 124, 136, 139-141 and 144 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

4. Reference is made to the following documents:

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International application No. PCT/US00/08586

D3: WO-A- 96 07427

D4: W.M. KALKA-MOLL ET AL.: 'BACTEROIDES FRAGILIS NCTC 9343 CAPSULAR POLYSACCHARIDE PS A AND THE EFFECT OF CHAIN LENGTH ON T CELL PROLIFERATION.' ABSTRACTS OF THE 98 TH GENERAL MEETING OF THE AMERICAN SOCIETY FOR MICROBIOLOGY, ATLANTA, US, MAY 17-21, 1998, vol. 98, 1998, page 123 XP002150693 WASHINGTON, US

5. None of the prior art documents cited in the search report discloses or suggests the use of *B. fragilis* PS A and *S. pneumonia* type 1 CP for reducing postoperative surgical adhesions.
- 5.1 Thus, as far as claims 109-111, 114-115, 117-119, 121-122, 124, 136, 138-141 and 144 relate to the aforementioned use of *B. fragilis* PS A and *S. pneumonia* type 1 CP, the subject matter of said claims is considered new and inventive over the cited prior art. Said claims do therefore meet the requirements of Art. 33(2) and 33(3) PCT.
6. For the assessment of the present claims 109-111, 114-115, 117-119, 121-122, 124, 136, 138-141 and 144 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.
7. Despite the fact that no opinion can be given regard to novelty, inventive step and industrial applicability of the present claims 1-64, 65-108, 112-113, 116, 120, 123, 125-135, 137, 142 and 143 because they have not been searched (see items 2 to 2.3 above), the following is to be noted for the sake of completeness:
 - 7.1 D3 (see e.g. summary of the invention on pp. 3-5; and p. 7) discloses that polymers having a particular structural motif that includes a positively charged free amino group and a negatively charged group on a repeating unit are capable of

inducing "cross-protection" against abscess formation by a variety of bacteria, and that said protective effect is mediated by T-cells. The polymers typically comprise repeating units of a charge motif characteristic of *B. fragilis* PS A. Preferably the polymer capsular is *isolated B. fragilis* PS A, although other naturally occurring polysaccharides can be modified to produce polymers having the aforementioned particular structural motif. As indicated in D3 (see p. 8, l. 9-10), the molecular weight of the polymers may vary from 0.5 to 20.000 kDa.

Thus, D3 anticipates the subject matter of the present claims 1-18, 65-98 and 101, as far as they cover polymeric compounds having the repeating structural charge motif disclosed in D3 and the use of said compounds for protecting against abscess formation and for activating T-cells.

- 7.2 D4 discloses the ability of *B. fragilis* PS A and small fractions thereof (with a molecular weight of 17 to 78 kDa) to stimulate T-cell proliferation.

Thus, D4 appears to anticipate the subject matter of the present claims 1-18 and 101, as far as they may cover the compounds disclosed in D4 or related ones.

Re Item VIII

Certain observations on the international application

8. Claims 1-144 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the technical contents of application. The particular effects of certain compounds shown in experimental examples of the application do not provide basis for generalization of said effects to all given compounds falling within the definitions given in the independent claims 1, 19, 37, 63 or 109.